Malignant Carcinoid Tumor

Altered Reactivity of the Skin to Serotonin in Two Patients

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• **Appropriately controlled tests were carried out in two cases of patients with carcinoid tumors and abnormal circulating levels of serotonin to verify a hypothesis that such patients would have a greater tolerance for exogenous serotonin than would normal persons. Contrary to the hypothesis, the patients had not less but more reaction to intradermal injection of serotonin than to histamine and also more reaction than normal persons.**

If this altered reactivity were to be observed consistently in large series of patients with malignant carcinoid disease, it might be used as a presumptive test.

IT HAS BEEN SUGGESTED that serotonin may be a naturally occurring vasodilator compound important in vascular homeostasis because of its ability to regulate peripheral neurogenic vasomotor tone.[4]

The syndrome of a carcinoid tumor with metastasis is now well recognized.[3] Unfortunately the many real and surmised biological functions of serotonin are not well understood.[4]

It was conjectured that a patient with a carcinoid tumor and abnormal circulating levels of serotonin would be able to tolerate exogenous serotonin to a greater degree than a normal person, and that if so the skin reactivity to serotonin as compared with reactivity to histamine would demonstrate the phenomenon. Tests in point were carried out in two cases.

REPORTS OF CASES

CASE 1. A white man 56 years of age, had flushing and peripheral cyanosis, episodic bouts of diarrhea and a large nodular liver. He had had no asthmatic-like bouts. No cardiac murmur could be heard. He received no medications in the week preceding skin testing. In roentgen studies of the upper gastrointestinal tract, pronounced hepatomegaly, with displacement of the stomach laterally and posteriorly, was noted. Excretion of 5-hydroxy-indole acetic acid in four 24-hour periods was as follows: July 17, 38 mg.; July 4, 52 mg.; June 28, 46 mg.; June 24, 45 mg. Biopsy of the liver at laparotomy confirmed the diagnosis.

CASE 2. A Negro woman 56 years of age had a grade II systolic murmur heard along the left sternal border, possible beginning bouts of diarrhea, and hepatomegaly. She had had no asthmatic-like bouts, no episodes of flushing or cyanosis, no symptoms of gastric ulcer. The patient was receiving tetracycline for a urinary tract infection. Excretion of 5-hydroxy-indole acetic acid for two 24-hour periods was as follows: September 9, 129 mg.; August 21, 118 mg. Biopsy of a yellow nodule on the liver through a peritineoscope was diagnostic of malignant carcinoid growth.

The materials used were: tuberculin syringes with No. 25 (French) needles; serotonin creatinine sulfate in physiological saline solution in dilutions of 1:1000 and 1:2000; histamine phosphate solution in physiological saline solution in dilution of 1:4000; and physiological saline solution.

Method: In each case two doses, one of .05 ml. of 1:1000 serotonin and one of 1:2000 serotonin, were administered intradermally in the flexor surface of the right forearm in a proximal and distal position, respectively. Histamine 1:4000 and a physiological saline solution control were placed on the left forearm in a similar fashion.

Results

CASE 1, right arm: The flexor surface of the forearm became diffusely erythematous and the finger tips became cyanotic. This occurred in slow progression and was complete in seven minutes. Then erythema slowly disappeared and the skin appeared completely normal in 25 minutes. No whealing was noted. The patient noticed pruritus without prompting. No systemic manifestations were noted. An hour later the same procedure on the other arm evoked the same response.

Left arm: At the site of histamine injection there was an area of erythema 3 cm. in diameter and a wheal 1.25 cm. in diameter, without pseudopod formation. The patient spontaneously complained of pruritus in this area. No reaction occurred at the site of saline solution injection. The histamine reac-

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tion resolved completely in two hours and fifteen minutes.

CASE 2, right arm: The two test areas become confluent in a patch of erythema 8 cm. by 10 cm. This reaction occurred quite rapidly, was complete in three minutes and had completely disappeared in seven minutes. No whealing was noted. Even with questioning, no subjective complaints were made regarding pain or pruritus. There was no fingertip cyanosis or manifestation of systemic effect.

Left arm: At the site of histamine injection an area of erythema 2.25 cm. in diameter and a wheal 2 cm. in diameter developed. One long trailing pseudopod was noted. The patient made no sensory complaint. No reaction was noted at the site of saline solution injection.

Twenty-five persons without disease were tested in a similar manner and the area erythema at the histamine injection was comparable in size to the area at the serotonin injection site. No whealing was noted in the area of intradermal serotonin in any of the controls. Eleven of the controls noted pruritus and pain to histamine and serotonin respectively. Nine reported no sensation of itch or pain. Two noted pain to both. One noted pruritus to both. One noted pain to histamine and pruritus to serotonin. One noted pruritus to histamine and no sensation to serotonin.[1,2]

Discussion

Contrary to the hypothesis, the two patients tested were not able to tolerate intradermal serotonin as well as normal persons. In supposition, one could postulate that patients with malignant carcinoid growths hyper-react to intradermal serotonin because their capillary threshold is altered by the exogenous increase of serotonin, more so than the normal.

If this altered reactivity of the skin is demonstrable in more than two patients with malignant carcinoid disease, a possible presumptive skin test is prognosticated.

Conclusion

Two patients with abnormal concentrations of 5-hydroxy-indole acetic acid in their urine had hyper-reactivity to intradermal injections of serotonin.

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REFERENCES

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Social Security Footnotes

OLD AGE AND SURVIVORS INSURANCE is a system under which the active workers and their employers are contributing the taxes necessary to pay benefits to their fellow citizens on the benefit rolls. The active workers now covered under the system must look for their own old-age benefits, not in any large measure to the Trust Fund, which is only a moderate buffer fund to cover temporary excess of benefit payments over tax receipts, but mainly to the willingness of the next generation of active workers to pay the increased taxes out of which the retirement benefits will come.

—From the Department of Public Relations, American Medical Association